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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,725	08/01/2003	David E. Wolf	205-007US2	2807

27791 7590 04/26/2007

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EXAMINER	
SHIBUYA, MARK LANCE	
ART UNIT	**PAPER NUMBER**
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,725	WOLF ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya, Ph.D.	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66,68 and 70-138* is/are pending in the application.

4a) Of the above claim(s) *1-58 and 74-117* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59-66 and 118-138* is/are rejected.

7)☒ Claim(s) *68* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/5/04; 9/13/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

1. Application No. 10632725 (20040082080 A1): Claims 1-66, 68, 70-138 are pending. Claims 67 and 69 are newly canceled. Claims 118-138 are newly added. Claims 1-58 and 74-117 are withdrawn as drawn to a non-elected invention. Claims 68 and 70-73 are withdrawn as drawn to a non-elected species. Claims 59-66 and 118-138 are examined.

2. The applicant's Reply, entered 10/23/2006, has been considered. Rejections and/or objections not reiterated from the previous Office action, mailed 7/21/2006, are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Nucleotide/Amino Acid Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e). Applicant is required to comply with the

corrections for the sequence listing as per above as part of a complete response to this official action. Applicant is requested to return a copy of the attached Notice to Comply with the response.

The specification at p. 31 discloses nucleotide sequences, but a Sequence Listing in paper and computer readable form has not been placed in the file. See also, infra, objections to the specification.

Election/Restrictions

3. Applicant's election with traverse of the species of bacterium in the reply filed on 2/9/2007 is acknowledged. The traversal is on the ground(s) that do not fully understand what is being asked of them. This is not found persuasive because the species are independent or distinct because different pathogens have materially different structures, functions and effects, including size. It is noted that in the method of the instant invention, dimension is a limitation, as in the subvolume through which the "pathogen" travels. Furthermore, in applicant's reply, entered 10/23/2006, to the previous Office action, mailed 7/21/2006, applicant traversed the cited prior art reference of Rigler et al., in part by arguing "[a] molecule is not a pathogen. A pathogen is an organism. In addition, a pathogen is an agent that causes a disease state." Reply at p. 25. Therefore, the examiner respectfully submits that applicant's arguments may be considered to show that the various species of pathogen are not obvious variants of each other, in the context of the claimed invention. In regard to claim 68, absent

argument or evidence to the contrary, a pathogen spore is materially different in form from a bacteria, as in the elected species.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 68 and 70-73 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/9/2007.

5. Claims 1-58 and 74-117 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/21/2006.

Priority

6. This application, 10/632,725, filed 8/1/2003, claims benefit of U.S. Provisional Application Serial No. 60/461,394, filed Apr. 8, 2003, U.S. Provisional Application Serial No. 60/430,273 filed Dec. 2, 2002, and U.S. Provisional Application Serial No. 60/400,503 filed Aug. 1, 2002.

7. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional

application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Provisional Application No.s 60/461,394, filed 4/8/2003; and 60/400,503, filed 8/1/2002, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Provisional Application No.s 60/461,394, filed 4/8/2003 and 60/400,503, filed 8/1/2002, do not provide support for methods of assaying for a pathogen in a sample, comprising antibodies. Therefore, the instant application has an effective filing date of **12/2/2002**, which is the filing date of Provisional Application Serial No. 60/430,273.

Response to Arguments

Applicant argues that the Office action, mailed 7/21/2006, did not specify the claims that do not satisfy the requirements of 35 USC 112, first paragraph.

Applicant's arguments, entered 10/23/2006, have been fully considered but they are not persuasive. The claims currently examined do not find support in 60/461,394, filed 4/8/2003 and 60/400,503, filed 8/1/2002. These said provisional applications do not disclose or suggest assaying for a pathogen in a sample.

Information Disclosure Statements

8. The information disclosure statement (IDS), filed 6/9/2004, fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the citation to the International Preliminary Examination Report does not provide a publication year.

Response to Arguments

Applicant argues that the IPER is not prior art. Applicant's arguments, entered 10/23/2006, have been fully considered but they are not persuasive. The IPER has been considered but the citation remains non-initialed because no publication year has been provided.

9. The citations AB, AC, AD, AE of the information disclosure statements (IDS), filed 2/5/04, have been initialed; the references cited to by said citations were previously considered.

10. The information disclosure statement (IDS) submitted on 9/13/06 was filed after the mailing date of the non-final rejection on 7/21/2006. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Objections to the Specification

11. The disclosure is objected to because of the following informalities: The instant specification at p. 31 recites sequences that must be identified by sequence identifiers.

Appropriate correction is required.

Withdrawn Objections/Rejections to the Claims

12. The following objections/rejections are withdrawn in view of applicant's arguments and amendments to the claims.

13. Claims 59-69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is withdrawn, in part, and maintained in part, (see below rejection under 35 USC 112, second paragraph.

New Claim Objections

14. Claim 68 is objected to because of the following informalities: Claim 60 states in part "pathogen spore,.". Appropriate correction is required.

New Claim Rejections - 35 USC § 112, First Paragraph

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 132-137 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is for new matter.

This rejection is necessitated by applicant's amendments to the claims.

Claims 132-137 state limitations drawn to analyzing occurring over particular ranges of seconds. These limitations do not appear to find support in the specification as filed. Applicant must point with particularity as to where these limitations are to be found in the specification as filed.

17. Claims 59-66 and 118-138 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is for lack of written description.

This rejection is necessitated by applicant's amendments to the claims.

The claims are drawn to methods of assaying for a pathogen in a sample, said method comprising: exciting said sample with radiation, said sample comprising at least one pathogen; at least one probe, and at least one fluorescent tag; measuring the fluorescence from a subvolume of said excited sample; and analyzing the fluctuations of said fluorescence that are due to the diffusion or flow of said pathogen through said subvolume; and variations thereof.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

One of skill in the art cannot envision the methods comprising the genus of probes and the genus of pathogens, such that analyzing the fluctuations of fluorescence that are due to the diffusion or flow of said pathogens through a subvolume, would result in the assaying for any species of pathogen. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The antibody probes taught by the specification do not represent an representative number of species adequate to describe identifying the genus of any pathogen using the claimed method. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

The reference of Robbins and Cotran, Pathologic Basis of Disease, Second Edition, W.B. Saunders Co., Philadelphia, (1979), at pp. 22-26, teach numerous pathogens, including biologic agents. Robbins et al., at p. 25, stress that, for example, whether an agent is a pathogen, is dependent not only upon the virulence of the agent itself, but also the susceptibility of the host. It is unpredictable that analysis of the diffusion or flow of, e.g., a bacteria through a subvolume, would allow identification of the bacteria as a pathogen. It is noted that claim 60 does not require that the specificity of the probe be specified.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112, Second Paragraph

Maintained Rejections

18. Claims 59, 118-121, 124-126, 130-132, 134 and 136 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is reiterated for the reasons of record as set forth in the previous Office action. This rejection is necessitated by applicant's amendments to the claims.

Claim 59 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: determining the presence or absence of the pathogen.

Claim 63 recites the limitation "said first fluorescent tag" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Response to Arguments

Applicant argues that claim 59 states a method recited steps for a useful method.

Applicant's arguments, entered 10/23/2006, have been fully considered but they are not persuasive. Claim 59 is vague and indefinite because it is unclear that the method steps are for the method as set forth in the preamble.

New Rejections

19. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. Claims 131-133 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's usage of the language of "identity of said pathogen is unknown" appears to read upon a mental step. It unclear as to who or what the identity of the pathogen is "unknown" or the distinguishing physical feature of a pathogen that is unknown. It is unclear as to whether the language refers to a mental step or attempts to refer to a structural limitation of the claimed product. It is not disputed that applicant may be their own lexicographer. The examiner does not argue that the term is repugnant to the usual usage in the art. Rather, it is that claim 131 does not reasonably apprise of one skill in the art as to the metes and bounds of the claimed invention.

Claims 132 and 133 recite the limitation wherein the analyzing occurs over a period of seconds, which renders the claims vague and indefinite, because the limitation is tantamount to claiming that the analyzing occurs over a period of time, and so would not apprise one of skill in the art of the metes and bounds of the claimed invention.

Maintained Claim Rejections - 35 USC § 102

21. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

22. Claims 59-66 and 118-125, 127, 128, 130-133, and 138 are rejected under 35 U.S.C. 102(e) as being anticipated by Rigler et al., US 6,582,903 B1.

This rejection is maintained for the reasons of record as set forth in the previous Office action. That rejection is copied below for the convenience of the reader. This rejection is necessitated by applicant's amendments to the claims.

The claims are drawn to a method of assaying for the presence of a pathogen component in a sample, said method comprising: exciting a sample with radiation, said sample comprising at least one probe capable of binding a predetermined pathogen component, and at least one fluorescent tag; measuring the fluorescence from a subvolume of said sample; analyzing the fluctuations of said fluorescence; and determining the presence or absence of said pathogen component; and variations thereof.

Rigler et al., throughout the patent, and at col. 16, line 47, teaches detecting pathogens reading on method of assaying for the presence of a pathogen component in a sample; Rigler et al., e.g., at col. 1, lines 55-58, teach fluorescence correlation spectroscopy (FCS) using chromophorous molecular structures having fluorescence properties, reading on fluorophores; wherein the fluorophorous molecules in solution are exposed to the intense exciting light of a laser, (Rigler et al. at col. 2, lines 21-24), which reads on exciting a sample with radiation, said sample comprising a complex of a target molecule to be detected and a labeled test reagent, (Rigler et al., at col. 7, lines 14-27), the receptor molecules/ligands, (Rigler et al., col. 8, lines 50-64), including antibodies, which reads further on at least one probe capable of binding a predetermined pathogen component, and at least one fluorescent tag, (Rigler et al., col. 13, lines 45-62; col. 18, line 41-col. 19, line 2); measuring fluorescence from a volume element, reading on measuring the fluorescence from a subvolume of said sample, (see col. 12, line 62-col. 13, line 10; col. 13, line 62-col. 14, line 45); analyzing the fluctuations of said fluorescence, (Rigler et al., at col. 2, line 7-20); and determining the presence or absence of said pathogen component, (Rigler at col. 8, lines 25-30; col. 16, lines 36-47).

Rigler et al. at col. 2, line 7-31, teach that spectroscopic methods for measuring fluorescence fluctuations are employed in fluorescence correlation spectroscopy. In considering the disclosure of the instant application in regards to measuring fluctuations in fluorescence intensity in fluorescence correlation spectroscopy, the examiner respectfully notes that the instant specification states:

> Fluorescence correlation spectroscopy (FCS) is a single molecule detection method that measures the fluctuations in fluorescence intensity in a small (e.g., femtoliter) confocal volume. FCS employs a tightly focused laser beam to define the confocal volume. The diffusion of fluorescently labeled particles into and out of the illuminated volume determines the fluorescence intensity fluctuation patterns. From this data, one can extract both qualitative information and quantitative information on the molecule being studied. Such qualitative information includes, e.g., the presence or absence of molecular interaction; such quantitative information includes diffusion time, stoichiometry of the interactions, concentration of the interacting particles and the kinetics of the interaction.

Specification at pp. 1-2, bridging paragraph.

Rigler et al., at col. 12, lines-22, teach at least two differently labeled test reagents which will bind to different sequence segments of an analyte, and teach cross correlation of a chromophore 1 and a chromophore 2, (col. 13, line 45-col. 14, line 9), reading on a plurality of unique fluorescently tagged probes, as in claims 62 and 63. Rigler at col. 11, line 45-col. 12, line 22, teaches determining the crosscorrelation function and the autocorrelation function of a sample, reading on claim 64. Rigler at col. 25, lines 10-25, col. 35, lines 57-65, teach pathogens that comprise bacteria or virus, as in claims 65 and 66.

The claims are drawn to methods of assaying for a pathogen in a sample, said method comprising: exciting said sample with radiation, said sample comprising at least one pathogen; at least one probe, and at least one fluorescent tag; measuring the fluorescence from a subvolume of said excited sample; and analyzing the fluctuations of said fluorescence that are due to the diffusion or flow of said pathogen through said subvolume; and variations thereof. These claims are anticipated by Rigler et al., for the reasons as set forth above.

Response to Arguments

Applicant argues Rigler does not disclose a method for assaying a pathogen in a sample, in a sample volume that includes one pathogen. Applicant's representative states: "A molecule is not a pathogen. A pathogen is an organism. In addition a pathogen is an agent that causes a disease state", (Reply at p. 25).

Applicant's arguments, entered 10/23/2006, have been fully considered but they are not persuasive.

Firstly, as stated in the previous Office action, claims must be given their broadest reasonable interpretation consistent with the supporting description. In re Hyatt, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). The claims are drawn to pathogens. See, *e.g.*, *Invitrogen Corp v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 1997); and MPEP 211.03. The claims and the specification do not provide a limiting definition for the term "pathogen". Dorlands's Illustrated Medical Dictionary, Twenty-fifth Edition, Saunders, Philadelphia (1979) at p. 1148, defines the term pathogen as "any disease-producing microorganism **or**

material." Emphasis added. Therefore, the examiner respectfully submits that the term pathogen, when given its broadest reasonable interpretation, is taught by reference of Rigler.

The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness."). MPEP 2145. Applicant's representative states: "A molecule is not a pathogen. A pathogen is an organism. In addition a pathogen is an agent that causes a disease state", (Reply at p. 25). The examiner respectfully submits that this is merely argument that is insufficient as objective evidence.

23. Claims 59-66 and 118-125, 127, 128, 130-133, and 138 are rejected under 35 U.S.C. 102(b) as being anticipated by Rigler, Journal of Biotechnology, vol. 41 (1995), pp. 177-186.

This rejection is maintained for the reasons of record as set forth in the previous Office action. That rejection is copied below for the convenience of the reader. This rejection is necessitated by applicant's amendments to the claims.

Rigler (1995), throughout the publication and abstract, and at pp. 182-184, teach methods of assaying for the presence of a pathogen component in a sample, said

method comprising: exciting a sample with laser radiation, (Rigler (1995) at p. 178, Fig. 1), said sample comprising at least one probe (Rigler (1995) at p. 178, para 2) capable of binding a predetermined pathogen component, such as hepatitis B and C or HIV and virus that is M13 bacteriophage, (Rigler (1995) at pp. 182-193, bridging paragraph, and as in claim 65) using several fluorescence labeled primers in the form of a cocktail, (also reading on claim 62), reading on methods comprising at least one fluorescent tag, and measuring the fluorescence fluctuations from an extremely small volume element, (Rigler (1995), at p. 177, para 1-2), which reads on a subvolume of said sample and analyzing the fluctuations of said fluorescence, and determining the presence or absence of said pathogen component, (Rigler (1995) at pp. 182-193, bridging paragraph).

Rigler (1995), at p. 182, Fig. 6, teaches cross-correlation in two colors, reading on a plurality of probes with different fluorophore tags, and e.g., at p. 180, teach autocorrelations, as in claims 62-64.

Response to Arguments

Applicant argues Rigler does not disclose a method for assaying a pathogen in a sample, in a sample volume that includes one pathogen. Applicant's representative states: "A molecule is not a pathogen. A pathogen is an organism. In addition a pathogen is an agent that causes a disease state", (Reply at pp. 25, 29).

Applicant's arguments, entered 10/23/2006, have been fully considered but they are not persuasive.

Firstly, claims must be given their broadest reasonable interpretation consistent with the supporting description. In re Hyatt, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). The claims are drawn to pathogens. See, *e.g.*, *Invitrogen Corp v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 1997); and MPEP 211.03. The claims and the specification do not provide a limiting definition for the term "pathogen". Dorlands's Illustrated Medical Dictionary, Twenty-fifth Edition, Saunders, Philadelphia (1979) at p. 1148, defines the term pathogen as "any disease-producing microorganism **or material**." Emphasis added. Therefore, the examiner respectfully submits that the term pathogen, when given its broadest reasonable interpretation, is taught by reference of Rigler.

The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness."). MPEP 2145. Applicant's representative states: "A molecule is not a pathogen. A pathogen is an organism. In addition a pathogen is an agent that causes a disease state", (Reply at p. 25). The examiner respectfully submits that this is merely argument that is insufficient as objective evidence.

24. Claims 59-66 and 118-125, 127, 128, 130-138 are rejected under 35 U.S.C. 102(b) as being anticipated by Weiner et al., Digestion, 2000, vol. 61, pp. 84-89.

This rejection is maintained for the reasons of record as set forth in the previous Office action. That rejection is copied below for the convenience of the reader. This rejection is necessitated by applicant's amendments to the claims.

Weiner et al., throughout the publication, abstract, and at para 1, teach measuring serum hepatitis C virus (HCV) RNA, and teach a fluorescence correlation spectroscopy method (p. 85, Methods, para 7) for assaying the pathogen, HCV in a sample, reading on assaying for the presence of a pathogen component in a sample, said method comprising: exciting a sample with argon-ion laser, radiation, said sample comprising Cy3-labeled amplimers for HCV RNA, (Weiner et al., at p. 85, para 8), reading on a at least one probe capable of binding a predetermined pathogen component, and at least one fluorescent tag; measuring the fluorescence from a subvolume of said sample and measuring diffusion times, (p. 85, para 8), reading on analyzing the fluctuations of said fluorescence; and determining the presence or absence of said HCV.

Response to Arguments

Applicant argues Wiener does not disclose a method for assaying a pathogen in a sample, in a sample volume that includes one pathogen. Applicant's representative states: "The RNA of hepatitis C virus is not a pathogen. Therefore Weiner et al. do not teach a sample that includes a pathogen", (Reply at p 29).

Applicant's arguments, entered 10/23/2006, have been fully considered but they are not persuasive.

Firstly, claims must be given their broadest reasonable interpretation consistent with the supporting description. In re Hyatt, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). The claims are drawn to pathogens. See, *e.g.*, *Invitrogen Corp v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 1997); and MPEP 211.03. The claims and the specification do not provide a limiting definition for the term "pathogen". Dorlands's Illustrated Medical Dictionary, Twenty-fifth Edition, Saunders, Philadelphia (1979) at p. 1148, defines the term pathogen as "any disease-producing microorganism **or material**." Emphasis added. Therefore, the examiner respectfully submits that the term pathogen, when given its broadest reasonable interpretation, is taught by reference of Weiner et al.

The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness."). MPEP 2145. Applicant's representative states: "The RNA of hepatitis C virus is not a pathogen", (Reply at p. 29). The examiner respectfully submits that this is merely argument that is insufficient as objective evidence.

25. Claims 59-66 and 118-125, 127, 128, 130-138 are rejected under 35 U.S.C. 102(b) as being anticipated by Walter et al., Proc. Natl. Acad. Sci., USA, November 1996, vol. 93, pp. 12805-12810.

This rejection is maintained for the reasons of record as set forth in the previous Office action. That rejection is copied below for the convenience of the reader. This rejection is necessitated by applicant's amendments to the claims.

Walter et al., throughout the publication and abstract and at p.12805, para 1-2, teach a method of assaying for the presence of a *Mycobacterium tuberculosis* pathogen component in a sample, said method comprising: exciting a sample with laser radiation, 9P. 12805, para 1), said sample comprising at least one primer (see Table 1, p. 12807) capable of binding a *M. tuberculosis* DNA pathogen component, and at least one fluorescent rhodamine tag; measuring the fluorescence from a investigated volume (Walter et al. at p. 12805, para 1), reading on a subvolume of said sample; analyzing the fluctuations of said fluorescence, (Walter et al. at p. 12805, para 1); and determining the presence or absence of said pathogen component.

Response to Arguments

Applicant argues Walter et al., does not disclose a method for assaying a pathogen in a sample, in a sample volume that includes one pathogen. Applicant's representative states: "A DNA is not a pathogen. Walter et al. thus fail to teach the method of claim 60", (Reply at p 31).

Applicant's arguments, entered 10/23/2006, have been fully considered but they are not persuasive.

Firstly, claims must be given their broadest reasonable interpretation consistent with the supporting description. In re Hyatt, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). The claims are drawn to pathogens. See, *e.g.*, *Invitrogen Corp v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 1997); and MPEP 211.03. The claims and the specification do not provide a limiting definition for the term "pathogen". Dorlands's Illustrated Medical Dictionary, Twenty-fifth Edition, Saunders, Philadelphia (1979) at p. 1148, defines the term pathogen as "any disease-producing microorganism **or material**." Emphasis added. Therefore, the examiner respectfully submits that the term pathogen, when given its broadest reasonable interpretation, is taught by reference of Walter et al.

The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness."). MPEP 2145. Applicant's representative states: "A DNA is not a pathogen", (Reply at p. 29). The examiner respectfully submits that this is merely argument that is insufficient as objective evidence.

Claim Rejections - 35 USC § 103

26. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

27. Claims 59-66 and 118-125, 127, 128, 130-138 are rejected under 35 U.S.C. 103(a) as being unpatentable by **Kask**, US 6,515,289, in view of **Lahiri et al.**, US 2003/0138853 A1.

This rejection is maintained for the reasons of record as set forth in the previous Office action. That rejection is copied below for the convenience of the reader. This rejection is necessitated by applicant's amendments to the claims.

Kask, US 6,515,289, throughout the patent, and at col. 1, lines 5-13, teaches methods of detecting substances in a sample, said method comprising: exciting a sample with radiation, (Kask at col. 3, line 63-col. 4, line 9), said sample comprising a labeled reactant that binds to a substance, reading on at least one probe capable of binding a predetermined component, and at least one fluorescent tag (col. 8, lines 8-29); Kask at, e.g., col. 2, lines 47-63, teaches monitoring intensity fluctuations of radiation emitted by molecules in a measurement volume, reading on measuring the fluorescence from a subvolume of said sample and analyzing the fluctuations of said fluorescence; and determining the presence or absence of said component, including viruses and bacteria, (col. 6, lines 31-48; and as in claims 65 and 66).

Kask at col. 1, lines 23-teach that spectroscopic methods for measuring fluorescence fluctuations are employed in fluorescence correlation spectroscopy (FCS).

In considering the disclosure of the instant application in regards to measuring fluctuations in fluorescence intensity in fluorescence correlation spectroscopy, the instant specification states:

> Fluorescence correlation spectroscopy (FCS) is a single molecule detection method that measures the fluctuations in fluorescence intensity in a small (e.g., femtoliter) confocal volume. FCS employs a tightly focused laser beam to define the confocal volume. The diffusion of fluorescently labeled particles into and out of the illuminated volume determines the fluorescence intensity fluctuation patterns. From this data, one can extract both qualitative information and quantitative information on the molecule being studied. Such qualitative information includes, e.g., the presence or absence of molecular interaction; such quantitative information includes diffusion time, stoichiometry of the interactions, concentration of the interacting particles and the kinetics of the interaction.

Specification at pp. 1-2, bridging paragraph.

Kask, at col. 8, lines 9-50, teaches a plurality of primers labeled with different dyes, reading on a plurality of unique fluorescently tagged probes, as in claims 62 and 63. Kask at, e.g., col. 5, line 65-col. 6, line 3, teach cross-correlation and auto-correlation functions, and combinations thereof, as in claim 64.

Kask et al. do not teach the detection of pathogens.

Lahiri et al., US 2003/0138853 A1, throughout the publication, and at para [0077] teach assay for the presence of a pathogen for diagnosis; and at para [0071], teaches using fluorescence correlation spectroscopy (FCS) as a detection method.

It would have been *prima facie* obvious, at the time the invention was made, for one of ordinary skill in the art to have made and used a method of assaying for the presence of a pathogen component in a sample using fluorescence fluctuation methods, such as FCS.

One of ordinary skill in the art would have been motivated to make and use a method of assaying for the presence of a pathogen component in a sample by measuring fluorescence fluctuation, because Lahiri et al. teach using FCS for detecting pathogens for diagnosis and because Kask, at col. 7, lines 37-42, teach using FCS for high throughput screening, and for diagnostic purposes, and teaches the detection of viruses and bacteria, as stated above.

One of ordinary skill in the art would have had a reasonable expectation of success in assaying for the presence of a pathogen by measuring fluorescence fluctuations because Kask et al. teach measuring bacteria and virus by such methods.

Response to Arguments

Applicant argues that a prima facie case of obviousness has not been made because the references do not describe all elements, in particular, the references do not disclose pathogens. Applicant argues that the reference of Lahiri et al. does not explain what is meant by "derived from" a body fluid. Applicant argues that the term "derived from" does not inherently mean that the sample includes a pathogen. Furthermore analytes indicative of pathogens could be, for example, antibodies to the pathogen, and not pathogens.

Applicant's arguments, entered 10/23/2006, have been fully considered but they are not persuasive.

Firstly, Lahiri et al., US 2003/0138853 A1, throughout the publication, and at para [0077] teach assay for the presence of a pathogen for diagnosis; and at para

[0071], teaches using fluorescence correlation spectroscopy (FCS) as a detection method. Applicant's argument ignores the plain meaning of the reference.

Claims must be given their broadest reasonable interpretation consistent with the supporting description. In re Hyatt, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). The claims are drawn to pathogens. See, *e.g.*, *Invitrogen Corp v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 1997); and MPEP 211.03. The claims and the specification do not provide a limiting definition for the term "pathogen". Dorlands's Illustrated Medical Dictionary, Twenty-fifth Edition, Saunders, Philadelphia (1979) at p. 1148, defines the term pathogen as "any disease-producing microorganism **or material**." Emphasis added. Therefore, the examiner respectfully submits that the term pathogen, when given its broadest reasonable interpretation, is taught by the combination of the references of Kask and Lahiri et al.

Conclusion

28. Claims 59-66 and 118-138 stand finally rejected. Claim 68 is objected to.

29. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

30. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Shibuya, whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. J. Douglas Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark L. Shibuya, Ph.D.
Primary Examiner
Art Unit 1639

Notice to Comply	Application No.	Applicant(s)
	10/632,725	WOLF
	Examiner	Art Unit
	SHIBUYA	1639

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☑ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☑ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: Please see attached sheets.

Applicant Must Provide:

☑ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☑ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☑ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510
For CRF Submission Help, call (571) 272-2501/2583.
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